

Seeking Harmony in Risk Assessment: ♪

Key Role for the Mode of Action ♪

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Mode of Action (MOA):

A Biological Basis for Risk Assessment Procedures

- # Establish MOA in animals
- # Establish relevance of animal model for human risk assessment
- # Provide guidance for selection of dose-response model

Mode of Action is a “sequence of key events and processes, starting with interaction of an agent with a cell, proceeding through operational and anatomical changes, and resulting in cancer formation.”

Mechanism of Action... “implies a more detailed understanding and description of events, often at the molecular level, than is meant by mode of action.”

Dose-response modeling is a two-step process.

1. Model observed data to point of departure (POD).
2. Extrapolate to exposures of interest using either:
 - a. by a straight line to the origin, or
 - b. by incorporating the cancer POD into the RfD/RfC calculation.

Harmonized, biologically based, and data-dependent procedures provide a less-fragmented, more integrated, and more biologically consistent approach to risk assessment that is more easily explained to stakeholders, including the general public.

Like all improvements in the quality of risk assessments and risk communication, the harmonization process should better inform Federal, State, and local decisionmakers.

